Haemophilus influenzae (Invasive)

Report Immediately

1) THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic Agent

Haemophilus influenzae (H.i.) disease is caused by small gram-negative coccobacilli that may be either encapsulated (types a–f) or unencapsulated (nontypeable). Type b (Hib) is the only kind for which there is a vaccine and for which control measures are considered necessary.

B. Clinical Description

Invasive H.i. disease may produce various clinical syndromes, including meningitis, bacteremia or sepsis, epiglottitis, pneumonia, septic arthritis, osteomyelitis, pericarditis, empyema, and abscesses. In contrast, mucosal infections such as bronchitis, sinusitis, and otitis, which can be caused by H.i., are considered noninvasive disease.

C. Reservoir

Humans are the only known host.

D. Modes of Transmission

H.i. is transmitted person-to-person by droplet or direct contact with nasopharyngeal secretions of an infected person. The most common portal of entry is the nasopharynx. Newborns can become infected by inhaling amniotic fluid or genital tract secretions containing the organism.

E. Incubation Period

The incubation period is unknown but probably short, 2–4 days.

F. Period of Communicability or Infectious Period

- **If not on antibiotic therapy**—as long as organisms are present in the upper respiratory tract, which may be for a prolonged period even without nasal discharge.
- **If on antibiotic therapy**—noncommunicable within 24–48 hours after starting effective antibiotic therapy.

The contagious potential of invasive H.i. disease is considered to be limited. However, certain circumstances, particularly close contact with a case (*e.g.*, in a household, daycare center, or institutional setting), can lead to outbreaks of Hib or direct secondary transmission of the disease. Asymptomatic carriage is known to occur.

G. Epidemiology

H.i. occurs worldwide. Invasive H.i. is most prevalent among children aged 2 months to 3 years and is unusual in healthy individuals over the age of 5 years. In the United States, peak incidence is in children 6–12 months of age. Secondary cases may occur in households, daycare centers, and other institutional settings.

Before the widespread use of Hib conjugate vaccines, *Haemophilus influenzae* type b (Hib) was a leading cause of bacterial meningitis in the United States among children <5 years of age and a major cause of other life-threatening invasive bacterial diseases in this age group. Meningitis occurred in approximately two-thirds of

children with invasive Hib disease, resulting in hearing impairment or severe permanent neurologic sequelae such as mental retardation, seizure disorder, cognitive and developmental delay, and paralysis in 15–30% of survivors. Approximately 5% of all cases were fatal. Invasive Hib disease now occurs in unvaccinated or undervaccinated children and adults. Type f is the most common other serotype causing invasive infections in the US.

Invasive disease has been more frequent in boys, African Americans, Alaskan Eskimos, Apache and Navajo Indians, child care center attendees, children living in overcrowded conditions, and children who were not breastfed. Unimmunized children, particularly those younger than 4 years of age, who are in prolonged close contact (such as in a household setting) with a child with invasive Hib disease, are at an increased risk for invasive Hib disease. Other factors predisposing to invasive disease include sickle cell disease, asplenia, HIV infection, certain immunodeficiency syndromes, and malignant neoplasms.

2) REPORTING CRITERIA AND LABORATORY TESTING SERVICES

A. What to Report to the Massachusetts Department of Public Health

- A case clinically compatible with invasive H.i. (*e.g.*, with meningitis, bacteremia, epiglotittis, or pneumonia), as diagnosed by a healthcare professional, or
- Isolation (culture) of H.i. from a normally sterile body site (blood, cerebrospinal fluid (CSF), or less commonly joint, pleural, or pericardial fluid), or
- Detection of Hib antigen in CSF.

B. Laboratory Testing Services Available

Confirmation and serotyping of *Haemophilus influenzae* isolates are available at the Massachusetts State Laboratory Institute (SLI). All strains of H.i. isolated from normally sterile sites must be serotyped in order to identify the strain and to differentiate between serotype b and other serotypes, for which there are no control measures. Subcultures should be sent with a requisition form to the SLI Reference Laboratory (reachable at 617-983-6607).

Note: Positive antigen results from urine and/or serum samples are not reliable for diagnosis of H.i. disease and should not be used as a substitute for culture results.

3) DISEASE REPORTING AND CASE INVESTIGATION

A. Purpose of Surveillance and Reporting

- To ensure that all cases of invasive H.i. are typed and to identify all cases of Hib.
- To identify household and daycare contacts of Hib cases who need antimicrobial prophylaxis and/or immunization and to prevent further spread of the disease for Hib cases.
- To distinguish between failure to vaccinate and vaccine failure.

B. Laboratory and Healthcare Provider Reporting Requirements

Refer to the lists of reportable diseases (at the end of this manual's introductory section) for information.

Note: Due to the potential severity of invasive *Haemophilus influenzae*, the Massachusetts Department of Public Health (MDPH) requests that information about any case be **immediately reported** to the local board of health where diagnosed. If this is not possible, call the MDPH Division of Epidemiology and Immunization at (617) 983-6800 (weekdays) or (617) 983-6200 (nights/weekends).

C. Local Board of Health Reporting and Follow-Up Responsibilities

1. **Reporting**

MDPH regulations (*105 CMR 300*) stipulate that each local board of health must report the occurrence of any suspected or confirmed case of invasive H.i. disease, as defined by the reporting criteria in Section 2) A. MDPH requests that information about any suspect or known case of invasive *Haemophilus influenzae* be **immediately reported** to the MDPH Division of Epidemiology and Immunization, Surveillance Program by calling (617) 983-6800 (weekdays) or (617) 983-6200 (nights/weekends).

After the initial notification to MDPH, the local board of health shall promptly report each case, using the *Invasive Haemophilus influenzae Case Report Form* (available from the Division of Epidemiology and Immunization after January 2001). If a case of Hib is identified, the Massachusetts Immunization Program will become involved in the investigation and disease control recommendations, in collaboration with the local board of health. The local board of health should fax the lab report and/or other information to the Surveillance Program. The confidential fax number is (617) 983-6813.

2. **Case Investigation**

a. Ensure that typing of the H.i. isolate has been or is being done, preferably at the SLI. Call an epidemiologist at the Division of Epidemiology and Immunization at (617) 983-6800 for help.
b. Collect pertinent information (demographic, clinical, exposure setting, transmission setting, detailed immunization history, and other pertinent history on the case) and record on the *Invasive Haemophilus influenzae Case Report Form* (available from the Division of Epidemiology and Immunization after January 2001). To assess and prepare for the possibility of a type b case, it is important to pay special attention to the case's Hib vaccination history, whether the case had contact with another case of invasive Hib, whether a daycare setting is involved, and the ages and Hib vaccination histories of children exposed to the case in the household and daycare center.
c. If type b is identified, notify an epidemiologist at the Division of Epidemiology and Immunization (617-983-6800) and fax the case report form to the Division's Surveillance Program (617-983-6813) even if incomplete.
d. If type b is not identified, no additional control measures are necessary. Please complete the *Invasive Haemophilus influenzae Case Report Form* (available from the Division of Epidemiology and Immunization after January 2001) and mail in an envelope marked "Confidential" to the MDPH Division of Epidemiology and Immunization, Surveillance Program. The mailing address is:

Division of Epidemiology and Immunization
Surveillance Program, Room 241
305 South Street
Jamaica Plain, MA 02130

4) CONTROLLING FURTHER SPREAD

Control measures are for *Haemophilus influenzae* type b (Hib) *only*. There are **no** control measures for other types.

A. Isolation and Quarantine Requirements (*105 CMR 300.200*)

The Isolation and Quarantine Requirements (promulgated November 1998, printed July 1999) are out of date with respect to Hib. Current recommendations (as of 2000) are as follows:

Minimum Period of Isolation of Patient

Isolate the case until 24 hours after initiating appropriate antimicrobial treatment to eliminate carriage (currently only cefotaxime, ceftriaxone, and rifampin are known to eliminate carriage).

Minimum Period of Quarantine of Contacts
Where it has been determined that antimicrobial prophylaxis is necessary, children and staff should be excluded from the setting until rifampin has been started.

B. Protection of Contacts of a Case

1. **Isolate the case** until 24 hours after initiating appropriate antimicrobial treatment that eliminates carriage. Currently, only the treatment drugs cefotaxime and ceftriaxone are known to eradicate Hib from the nasopharynx. So, if the patient is treated with ampicillin or chloramphenicol instead, s/he must receive rifampin prophylaxis. Also, note that Hib disease does not necessarily confer immunity to subsequent disease. Immunize as follows:
   - **Children with invasive Hib disease at < 24 months of age—**immunize according to the age-appropriate schedule for unvaccinated children and as if they had received no prior doses. Begin 1 month after onset of disease or as soon as possible thereafter. For additional information, please refer to the table in Section 4) B. 3.
   - **Children with invasive Hib disease at ≥ 24 months of age—**no immunization is necessary, regardless of previous immunization status, because the disease probably induced a protective immune response and second episodes at this age are rare.

2. **Antimicrobial prophylaxis for close contacts.** Although several antibiotics are useful for *treatment* of invasive Hib disease and elimination of carriage in the case, rifampin is the appropriate drug to use for antibiotic *prophylaxis* of contacts. Several studies have shown that rifampin eradicated Hib carriage in ≥ 95% of contacts of primary Hib cases, including children in daycare facilities.

   When indicated, prophylaxis should be initiated as soon as possible. Most secondary cases in households occur in the first week after hospitalization of the index case. Prophylaxis of household contacts that begins ≥ 1 week after hospitalization of the case may still be of benefit, although initiation of prophylaxis beyond 4 weeks after that date is probably of limited utility. Prophylaxis is not recommended for pregnant women who are contacts because the effect of rifampin on the fetus has not been established.

Rifampin Prophylaxis against Hib	
Age Group	**Dosage/Schedule**
Infants < 1 month of age	10 mg/kg PO QD x 4 days
Children	20 mg/kg PO QD x 4 days (maximum: 600 mg/dose)
Adults	600 mg PO QD x 4 days

The risk of secondary disease in children attending child care centers appears to be lower than that observed for age-susceptible household contacts, and secondary disease in child care contacts is rare when all contacts are older than 2 years. Also, the efficacy of rifampin in preventing disease in child care groups is not established. Nevertheless, rifampin prophylaxis is recommended in certain situations, as indicated in the table below.

Indications and Guidelines for Rifampin Chemoprophylaxis for Contacts of Index Cases of Invasive *Haemophilus influenzae* Type b (Hib) Disease

Chemoprophylaxis recommended

- In certain index cases:
  - Index case, if treated with regimens other than cefotaxime or ceftriaxone. Chemoprophylaxis usually is provided just before discharge.
- In certain household situations:
  - All household contacts (except pregnant women),[1] irrespective of age, in households where at least 1 contact is < 48 months of age *and* is unimmunized or incompletely immunized[1]
  - All household contacts (except pregnant women),[1] irrespective of age, in households where a child is < 12 months of age, even if the primary series has been given
  - All household contacts (except pregnant women),[1] irrespective of age, in households with an immunocompromised child, irrespective of the child's Hib immunization status
- In certain child care situations:
  - Nursery and child care centers contacts where $\geq$ 2 cases occurred within 60 days, with $\geq$ 1 unimmunized or incompletely immunized child < 48 months of age[2,3]

Chemoprophylaxis *not* recommended

- In certain individuals:
  - Pregnant women
- In certain household situations:
  - Occupants of households with no children < 48 months of age other than the index patient
  - Occupants of households when all household contacts < 48 months of age have completed their Hib immunization series[4]
- In certain child care situations:
  - Nursery and child care contacts of 1 index case, when all contacts are > 24 months of age
  - Nursery and child care contacts of 1 index case, when all children < 48 months of age have completed their Hib immunization series[4]
  - Nursery and child care center contacts where $\geq$ 2 cases occurred within 60 days, when all children < 48 months of age have completed their Hib immunization series[4]

[1] Defined as persons residing with the index patient or nonresidents who spent $\geq$ 4 hours with the index case for $\geq$ 5 of the 7 days preceding the day of hospital admission of the index case.

[2] Only children who are age-appropriately immunized and on rifampin should be permitted to enter the childcare group during the time prophylaxis is given. Children enrolling in the day care center or other setting during the time prophylaxis is given should also receive rifampin, as should supervisory personnel.

[3] When a single case has occurred, the advisability of rifampin prophylaxis in exposed child care groups with unimmunized or incompletely immunized children is controversial, but many experts recommend no prophylaxis.

[4] Complete immunization is defined as having had $\geq$ 1 dose of conjugate vaccine at $\geq$ 15 months of age; 2 doses between 12 and 14 months of age; or a 2- or 3-dose primary series (number of doses required depends on vaccine type and age at initiation) when < 12 months with a booster dose at $\geq$ 12 months of age. Note that all infants (< 12 months of age) are by definition incompletely immunized.

3. **Ensure appropriate immunization of contacts.** The number of doses required is determined by the current age of the child and the number, timing, and type of Hib vaccine doses previously received. Unvaccinated and incompletely vaccinated children < 5 years of age should be scheduled for completion of the recommended age-specific immunization schedule (see definition of "complete immunization" in Footnote 1 of the table above). Infants should be placed on an accelerated schedule using minimum intervals between doses. Unvaccinated high-risk individuals ≥ 5 years of age should receive one dose.

   The accelerated schedule for situations in which an incompletely vaccinated child has been exposed follows:

Accelerated schedule for Hib vaccination—to be used for unvaccinated and incompletely vaccinated children (including all infants) after exposure to invasive Hib disease.				
Type of Hib vaccine	**Minimum age for first dose**	**Minimum interval from dose 1 to 2**	**Minimum interval from dose 2 to 3**	**Minimum interval from dose 3 to 4**
HbOC (HIB-TITER®)	6 weeks	1 month	1 month	This booster at ≥ 12 mo. of age and ≥ 2 mo. after previous dose
PRP-T (ActHIB®, OmniHIB®)	6 weeks	1 month	1 month	
PRP-OMP (PedVax-HIB®)	6 weeks	1 month	This booster at ≥ 12 mo. of age and ≥ 2 mo. after previous dose	Not required

4. **Conduct surveillance.** Careful observation of exposed contacts, especially children < 4 years of age, is essential. Those in whom a febrile illness develops should receive prompt medical attention, regardless of Hib vaccination status.

D. Preventive Measures

Routine childhood vaccination is the best preventive measure against Hib disease. Good personal hygiene (which consists of proper hand-washing, disposal of used tissues, not sharing eating utensils, etc.) is also important.

Please consult the chapter on *Haemophilus influenzae* in the *Red Book* of the American Academy of Pediatrics for a full discussion of vaccines, immunization schedules, and special circumstances. For example, children, including those ≥ 5 years of age, with underlying conditions predisposing them to Hib disease may need additional doses. Other relevant resources, including the MDPH's *Immunization Guidelines* and *Massachusetts Immunization Program-Supplied Vaccines and Patient Eligibility Criteria*, are available through the Division of Epidemiology and Immunization at (617) 983-6800 or (888) 658-2850.

A *Haemophilus influenzae type b Public Health Fact Sheet* for the general public can be obtained from the Division of Epidemiology and Immunization or through the MDPH website at <http://www.state.ma.us/dph/>. Click on the "Publications" link and scroll down to the Fact Sheets section.

ADDITIONAL INFORMATION

The following is the formal CDC surveillance case definition for invasive *Haemophilus influenzae*. It is provided for your information only, it is not necessary to use this information for reporting or investigating a

case. (CDC case definitions are used by the state health department and CDC to maintain uniform standards for national reporting.) For reporting to the MDPH, always use the criteria outlined in Section 2) A of this chapter.

Clinical description
Invasive disease caused by *Haemophilus influenzae* may produce any of several clinical syndromes, including meningitis, bacteremia, epiglotittis, or pneumonia.

Laboratory criteria for diagnosis
Isolation of H. influenzae from a normally sterile site (*e.g.,* blood or cerebrospinal fluid [CSF] or, less commonly, joint, pleural, or pericardial fluid).

Case classification
Probable: a clinically compatible case with detection of *H. influenzae* type b antigen in CSF.
Confirmed: a clinically compatible case that is laboratory confirmed.

Comment
Positive antigen test results from urine or serum samples are unreliable for diagnosis of *H. influenzae* disease.

REFERENCES

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